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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,724	02/09/2001	Joseph A. Kovacs	4239-58054	7526

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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	**PAPER NUMBER**
1634	10

DATE MAILED: 05/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,724	KOVACS ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the election filed March 8, 2002. Claims 1-24 are pending and have been examined on their merits.

Election/Restrictions

2. Applicant's election without traverse of Group I in Paper No. 8 is acknowledged. Applicant's election with traverse of SEQ ID NO: 13 in Paper No. 8 is acknowledged. The examiner has deemed for the purposes of the method claims, the restriction to a single sequence is not necessary and therefore has withdrawn the sequence restriction with respect to the method claims. This restriction is made FINAL.

Priority

3. This application claims priority to both PCT/US/99/18750, filed August 17, 1999 and provisional application 60/096,805, filed August 17, 1998.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

For example, page 9, lines 26-27, page 10, line 6 contain hyperlinks.

Claim Objections

5. Claims 6 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 6 are directed to primers which broadly comprise at least 15 contiguous nucleotides from a nucleic acid sequence having at least 90% sequence homology. The claim depends upon Claim 5 which is drawn, in part, to primers comprising at least 15 contiguous nucleotides from a sequence chose from a nucleic acid sequence having at least 91% sequence homology. Therefore, Claim 6 does not appear to further limit Claim 5 since Claim 5 is narrower in scope than Claim 6.

6. Claims 11-16 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 11-16 are directed to specific primers which broadly comprise specific SEQ ID NO:s. Each of the claims depend upon Claim 10 which are drawn to primers narrowly drawn. Therefore, Claims 11-16 do not appear to further limit Claim 10 since Claim 10 is narrower in scope than Claims 11-16.

7. Claims 21-22 are objected to because the claims depend upon one another. The claims are improperly dependent. Appropriate correction is required.

New Matter

8. Claims 3-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the amended claims, reference to "at least 79% sequence identity with residues 2821-3072 of HMSG35 (SEQ ID NO: 13)" and "at least 91% sequence homology" and "at least 91% sequence homology" to highly conserved regions are included. The amendment proposes that the new claim language can be found in a direct comparison of the highly conserved regions of the disclosed human- *P. carinii* MSG-encoding sequences and at least on page 9, line 10. However, the specification does not describe or discuses "at least 79% sequence identity with residues 2821-3072 of HMSG35 (SEQ ID NO: 13)" and "at least 91% sequence homology" to highly conserved regions.

With respect to Claim 3, 4, "at least 79% sequence identity with residues 2821-3072 of HMSG35 (SEQ ID NO: 13)" and "at least 91% sequence homology", the specification describes the conserved regions (page 17-18). The specification teaches that the full length clones are 74-91% identical at the nucleotide level (page 9 and page 21, lines 30-33). This description of the full length clones homology and the broad disclosure of the conserved regions does not provide adequate written description to the skilled artisan at the time the invention was made to recognize that the conserved

regions were at least 79% identical. Even in the event that applicant could argue that residues of 2821-3072 were inherently identical with the other sequences at a certain percentage, the amendment filed to illustrate the sequence comparison illustrates that each of the conserved regions from the sequences taught in the specification are greater than 84% identical with SEQ ID NO: 13, conserved region. The concept of "at least 79% sequence identity with residues 2821-3072 of HMSG35 (SEQ ID NO: 13)" does not appear to be part of the originally filed invention. Therefore, "at least 79% sequence identity with residues 2821-3072 of HMSG35 (SEQ ID NO: 13)" constitutes new matter.

With respect to Claims 5-7, "at least 91% sequence homology" to highly conserved regions, the specification teaches the conserved regions (page 17-18). The specification teaches that the full length clones are 74-91% identical at the nucleotide level (page 9 and page 21, lines 30-33). This description of the full length clones homology and the broad disclosure of the conserved regions does not provide adequate written description to the skilled artisan at the time the invention was made to recognize that the conserved regions were at least 91% identical. Further, a range of 74-91% identical is not equivalent to a range of at least 91% identical, namely 91-100% identity.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-22 are indefinite over the recitation "a highly conserved region". The term "highly conserved region" in claim 1 is a relative term which renders the claim indefinite. The term "highly conserved region" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what constitutes "highly" conserved. It is unclear whether the sequence must be conserved among all MSG protein encoding sequences, between two sequences, more than 70% homoglogy or more than 99% homology. Moreover, the description of the figure illustrates a boxed region which is depicted as the conserved amino acid region. This region is not inclusive of the regions delineated in the specification as the conserved regions (page 13). Thus, the metes and bounds of the claimed invention are unclear.

B) Claims 1-22 are indefinite because it is unclear whether the method is for detecting human *P. carinii* using human- *P. carinii* sequences or whether the method merely requires amplifying a highly conserved region within a human *P. carnii* sequence to determine the presence of such sequence in any organism. The recitation "amplifying a highly conserved region within a human *P. carinii* nucleic acid" does not make it clear whether the primers are taken from the human *P. carinii* region or whether the nucleic acid which is contacted with the primers is human *P. carinii* nucleic acid.

Claim 2 appears to require that the sample was a human *P. carinii* sample. Furthermore, Claims 1-22 are indefinite over the recitation "derived from" because this language does not particularly set forth whether the probes are limited to fragments of the human *P. carinii* MSG protein or can include sequences which were originally taken from the sequence but are then modified in sequence, i.e. by additions, deletions, substitutions, such that the probe sequences are not the same as human *P. carinii* MSG protein encoding sequences.

C) Claims 3-7 are indefinite because it is unclear whether the amplified region is at least 79% identical over the entire region of 2821-3072 of (SEQ ID NO: 13) or whether the amplified region may be smaller than 2821-3072 of SEQ ID NO: 13 where there is more than 79% identity between the smaller region. Furthermore, with respect to Claims 3-7, it is unclear how one would determine prior to amplification using primers derived from human P. carinii whether the resulting amplified sequence was at least 79% identical with another sequence. Using primers which are 100% identical with the sequence of SEQ ID NO: 13 would amplify any thing between the two primers. It is unclear how one would ensure that only regions with at least 79% identity between the 100% complementary primers were amplified. Thus, the metes and bounds of the claimed invention are unclear.

D) Claims 9-10 are indefinite over the recitation "wherein the pair of oligonucleotide primers consist of one upstream primer and one downstream primer" because it is unclear what the terms upstream and downstream are in relation to.

E) Claims 21 and 22 are indefinite because each of the claims depends upon the other. It is unclear what the claims are intended to encompass since they depend upon each other.

F) Claims 23-24 are indefinite over the recitation "derived from" because this language does not particularly set forth whether the probes are limited to fragments of the human *P. carinii* MSG protein or can include sequences which were originally taken from the sequence but are then modified in sequence, i.e. by additions, deletions, substitutions, such that the probe sequences are not the same as human *P. carin*ii MSG protein encoding sequences.

G) Claim 24 is indefinite over the recitation "the labeled probe" because "the labeled probe" lacks proper antecedent basis. Claim 23 does not recite a labeled probe. The rejection may be easily overcome by amending Claim 23 to require a labeled probe or adding a new claim to require that the probe is labeled.

H) Claims 22 and 24 are indefinite over the recitation "according to SEQ ID NO: 19". It is unclear what is encompassed by "according to". It is unclear whether according to is synonymous to comprising or consisting. Moreover, it is unclear whether according to SEQ ID NO: 19 encompasses according to all of SEQ ID NO: 19, a part of SEQ ID NO: 19. In the event that applicant intends to claim either consisting of or comprising SEQ ID NO: 19, this rejection may be easily overcome by deleting "a nucleic acid sequence according to" such that the claim would recite "wherein the probe is labeled and wherein the probe comprises SEQ ID NO: 19".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

10. Claims 1-2, 17, 19, 20, 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Wright (Gene, Vol. 167, No. 1-2, pages 185-189, 1995).

It is noted that the specification defines tissue samples taken from the oropharyngeal tract include samples from the lung of bronchial tissue (page 6, lines 20-25 of specification).

Wright et al. (herein referred to as Wright) teaches cloning and characterization of a conserved region of human and Rhesus macaque *Pneumocystis carinii* gpA. Wright teaches that *Pneumocystis carinii (Pc)* is a major opportunistic pathogen of

immunocompromised individuals, especially AIDS patients. Wright teaches that gpA is also known as MSG. Wright used conserved Cys-primers which amplified the nucleotide sequence which was 72% similar to the deduced aa sequnce recently reported for HPc gpA by Garbe and Stringer. Wright teaches the amplification of the human gpA gene using primers internal to the conserved Cys-primers. The primers amplified each of the three infected lung DNAs using hPc primers but not the unifected lung DNA (limitations of Claim 17). The samples were then tested by Southern blot analysis using a labeled oligo (page 187, col 1, Figure 2). Therefore, since Wright has taught every limitation of the claimed invention, Wright anticipates the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-2, 17, 19, 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stringer et al (J. Eukaryot. Microbiol. Vol. 40, pages 821-826, 1993) in view of Hogan (US Pat 5,595,874, January 1997).

This rejection is drawn to the claims which do not require any specific region of the MSG encoding sequences. It is noted that the specification defines tissue samples taken from the oropharyngeal tract include samples from the lung of bronchial tissue (page 6, lines 20-25 of specification).

Stringer et al. (herein referred to as Stringer) teaches an alignment of genes encoding antigenic surface glycoproteins in *Pneumocystis* from humans. Stringer teaches the human derived Pneumocystis was isolated from lung tissue taken at autopsy from AIDS patient (page 821, col 2)(limitations of Claim 17). Stringer teaches that divergence of the pgA/MSG gene families of *Pneumocystis* from different host species has been explored by the polymerase chain reaction and by nucleic acid hybridization (page 821, col 1). Stringer teaches that "divergence of gpA/MSG genes in *Pneumocystis* from rats and humans was also indicated by failure of a gpA/MSG gene from rat-derived organisms to hybridize to chromosomes from human-derived *Pneumocystis*, when hybridization was performed under high stringency conditions (pages 821, col 1). Stringer provides an alignment between two human-derived *Pneumocystis* gpA/MSG genes and corresponding regions from ferret and rat genes. The alignment illustrates conserved regions between the two human clones.

Stringer does not specifically teach detecting *Pneumocystis carinii* using PCR amplification to conserved regions.

However, Hogan et al. (herein referred to as Hogan) teaches the use of specific primers col. 6-7, lines 50-67, lines 1-12, and furthermore provides specific guidance for the selection of primers,

> "Once the variable regions are identified, the sequences are aligned to reveal areas of maximum homology or 'match'. At this point, the sequences are examined to identify potential probe regions. Two important objectives in designing a probe are to maximize homology to the target sequence(s) (greater than 90% homology is recommended) and to minimize homology to non-target sequence(s) (less than 90% homology to non-targets is recommended). We have identified the following useful guidelines for designing probes with the desired characteristics.
> First, probes should be positioned so as to minimize the stability of the probe:nontarget nucleic acid hybrid. This may be accomplished by minimizing the length of perfect complementarity to non-target organisms, avoiding G and C rich regions of homology to non-target sequences, and by positioning the probe to span as many destabilizing mismatches as possible (for example, dG:rU base pairs are less destabilizing than some others). Second, the stability of the probe:target nucleic acid hybrid should be maximized. This may be accomplished by avoiding long A and T rich sequences, by terminating the hybrids with G:C base pairs and by designing the probe with an appropriate Tm. The beginning and end points of the probe should be chosen so that the length and %G and %C result in a Tm about 2-10°C higher than the temperature at which the final assay will be performed. The importance and effect of various assay conditions will be explained further herein. Third, regions of the rRNA which are known to form strong structures inhibitory to hybridization are less preferred. Finally, probes with extensive self complementarity should be avoided."

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have designed probes and primers to conserved regions of the human gpA/MSG genes from human *Pneumocystis* in order to detect MSG protein encoding sequences. The ordinary artisan would have recognized, given the alignment of Stringer, that regions within the two human gpA/MSG genes were conserved between the two genes

and would have been motivated to have designed probes and primers to conserved regions as taught by Hogan to enable detection of human gpA/MSG nucleic acid sequences. The ordinary artisan would have been motivated to have detected human MSG encoding nucleic acid sequences because Pneumocystis causes pneumocystosis, an AIDS-associated pneumonia. The level of skill in the art for designing primers and probes to known conserved regions between sequences is extremely high. Therefore, the skilled artisan would have used primers, for example, from the 5' region which is highly conserved between the human sequences and from the 3' region which is also highly conserved to amplify the gpA/MSG gene region provided by Stringer.

13. Claims 1-11, 13, 14, 18-20, 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garbe et al. (Infection and Immunity, Vol. 62, No. 8, pages 3092-3101, August 1994) in view of Hogan (US Pat 5,595,874, January 1997).

Garbe et al. (herein referred to as Garbe) teaches the molecular characterization of clustered variants of gene encoding major surface antigens of human *Pneumocystis carinii*. Garbe teaches the nucleic acid sequence of one gene and three partial sequences from other genes. Garbe teaches sera from humans was analyzed (page 3093)(limitations of Claim 18). Garbe teaches a protein alignment for the msgI to msgIV and rat msg sequences. Garbe the amino acid sequence between 980-1030 of MsgI and MsgII are highly conserved regions. SEQ ID NO: 19 and 20 are within the region which is conserved between MsgI and MsgII. SEQ ID NO: 17 is 100% identical to the sequence illustrated in Figure 5.

Garbe does not specifically teach detecting *Pneumocystis carinii* using PCR amplification to conserved regions.

However, Hogan et al. (herein referred to as Hogan) teaches the use of specific primers col. 6-7, lines 50-67, lines 1-12, and furthermore provides specific guidance for the selection of primers,

> "Once the variable regions are identified, the sequences are aligned to reveal areas of maximum homology or 'match'. At this point, the sequences are examined to identify potential probe regions. Two important objectives in designing a probe are to maximize homology to the target sequence(s) (greater than 90% homology is recommended) and to minimize homology to non-target sequence(s) (less than 90% homology to non-targets is recommended). We have identified the following useful guidelines for designing probes with the desired characteristics.
> First, probes should be positioned so as to minimize the stability of the probe:nontarget nucleic acid hybrid. This may be accomplished by minimizing the length of perfect complementarity to non-target organisms, avoiding G and C rich regions of homology to non-target sequences, and by positioning the probe to span as many destabilizing mismatches as possible (for example, dG:rU base pairs are less destabilizing than some others). Second, the stability of the probe:target nucleic acid hybrid should be maximized. This may be accomplished by avoiding long A and T rich sequences, by terminating the hybrids with G:C base pairs and by designing the probe with an appropriate Tm. The beginning and end points of the probe should be chosen so that the length and %G and %C result in a Tm about 2-10°C higher than the temperature at which the final assay will be performed. The importance and effect of various assay conditions will be explained further herein. Third, regions of the rRNA which are known to form strong structures inhibitory to hybridization are less preferred. Finally, probes with extensive self complementarity should be avoided."

Hogan teaches labeling the oligonucleotide probe (col 8, lines 65-68)(limitations of Claim 20). As clearly illustrated in Example 1, Hogan teaches using a single stranded oligonucleotide which is labeled to detect the presence of the organism of interest. The oligonucleotide used in the detection assay is specific to the organism and does not cross react with closely related sequences (col 12)(limitations of Claim 23).

Similarly, Example 3, illustrates the detection of a complex of organisms using a labeled probe which is specific to the complex (col 17-18).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have designed probes and primers to conserved regions of the human gpA/MSG genes from human *Pneumocystis* in order to detect MSG protein encoding sequences. The ordinary artisan would have recognized, given the alignment of Garbe, that regions within the two human gpA/MSG genes were conserved between the two genes and would have been motivated to have designed probes and primers to conserved regions as taught by Hogan to enable detection of human gpA/MSG nucleic acid sequences. The ordinary artisan would have been motivated to have detected human MSG encoding nucleic acid sequences because *Pneumocystis* causes pneumocystosis, an AIDS-associated pneumonia, and adverse reactions to chemotherophy. The level of skill in the art for designing primers and probes to known conserved regions between sequences is extremely high. Therefore, the skilled artisan would have used primers, for example, from the region which is highly conserved between the human sequences namely amino acids 980-1030 to amplify the gpA/MSG gene region provided by Stringer. The skilled artisan would have been motivated to have designed primers which flank the conserved regions. These primers would clearly encompass primers comprising SEQ ID NO: 19 and SEQ ID NO: 20 since these primers lie in regions which are conserved between the human MSG gene sequences. With respect to SEQ ID NO: 17, the sequence is 100% identical with a known MSG gene sequence such that using the primer would facilitate detection of the presence of *P. carinii* as required by Claim 1.

14. Claims 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garbe et al. (Infection and Immunity, Vol. 62, No. 8, pages 3092-3101, August 1994) in view of Hogan (US Pat 5,595,874, January 1997) as applied to Claims 1-11, 13, 14, 18-20, 23-24 and further in view of Mullis et al. (US Pat. 4,683,195, July 1987).

The specification teaches that an Eco RI site was added to the sense primer (SEQ ID NO: 23) and an Xba I site to the antisense primer to facilitate subcloning (SEQ I DNO: 24) (page 24 of specification, lines 27-30).

Garbe nor Hogan specifically teach inserting a restriction site into SEQ ID NO: 23, 24.

However, Mullis teaches primers may be modified to assist the rapid and specific cloning of the mixture of DNAs produced by the amplification reaction. Mullis teaches modification of the same or different restriction sites are incorporated at the 5' ends of the primers to result in restriction sites at the two ends of the amplified products such that the amplified products, when cut, may be easily inserted into plasmid or viral vectors and cloned (col 15, lines 37-45).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the sequence taught by Garbe in view of Hogan for detection of human *P. carinii* with the teachings of Mullis to introduce known restriction sites into the primer to facilitate subsequent cloning. The ordinary artisan would have been motivated to have inserted known restriction sites into probes and primers designed for detection of *P. carinii* for the express benefit taught by Mullis for subsequent cloning.

15. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wright (Gene, Vol. 167, No. 1-2, pages 185-189, 1995) or Stringer et al (J. Eukaryot. Microbiol. Vol. 40, pages 821-826, 1993) in view of Hogan (US Pat 5,595,874, January 1997) as applied to Claims 1-2, 17, 19, 23 and further in view of Chary-Reddy (J. of Clin. Microb. Vol 34, No. 7, pages 1660-1665, July 1996)

Wright et al. (herein referred to as Wright) teaches cloning and characterization of a conserved region of human and Rhesus macaque *Pneumocystis carinii* gpA. Wright teaches that *Pneumocystis carinii (Pc)* is a major opportunistic pathogen of immunocompromised individuals, especially AIDS patients. Wrigth teaches that gpA is also known as MSG. Wright used conserved Cys-primers which amplified the nucleotide sequence which was 72% similar to the decuded aa sequnce recently reported for HPc gpA by Garbe and Stringer. Wright teaches the amplification of the human gpA gene using primers internal to the conserved Cys-primers. The primers amplified each of the three infected lung DNAs using hPc primers but not the unifected lung DNA (limitations of Claim 17). The samples were then tested by Southern blot analysis using a labeled oligo (page 187, col 1, Figure 2).

Neither Wright, Stringer, nor Hogan specifically teach the detection of *P. carinii* in blood samples.

However, Chary-Reddy teaches P. carinii was present in adrenal tissue, bond marrow, blood, and heartk, kidney, liver, lymph node, spleen and thyroid tissues.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the method of detection of *P. carinii* in lung tissue, as taught by Wright and Stringer, with the teachings of Chary-Reddy who teaches the presence of the organism in a multitude of other tissues. The ordinary artisan would be motivated to detect the organism in blood because blood is an easily obtainable sample which does not require waiting until the time of autopsy or death to sample. Sampling of blood for the detecting *P. carinii* may be done to determine whether a patient is infected such that the patient is susceptible to AIDS induced pneumonia.

Conclusion

16. No claims allowable.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of formal matters can be directed to the patent analyst, Pauline Farrier, whose telephone number is (703) 305-3550.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Goldberg
May 14, 2002

Lisa B. Arthur

LISA B. ARTHUR
PRIMARY EXAMINER
GROUP 1800 1600